REMARKS

Applicant has canceled Claims 31-34. Applicant has amended Claims 28, 29, 35, 37, 40 and 42 for the purposes of clarification. Said amendments add no new matter and are fully supported by the Specification. Specifically, support for the use of the word "polynucleotide" can be found in the Specification on page 6, lines 7-8 and for "introduction of an exogenous polynucleotide encoding an IFNAR2c polypeptide" on Page 5, lines 8-10.

Claim Objection

The Examiner has objected to Claim 42 because of a missing article "a" in front of the term "human IFNAR2c" on line 5 of the claim. Applicant has amended Claim 42 to include an "a" at this position.

Rejection under 35 U.S.C. §112, first paragraph

The Examiner has rejected Claim 42, under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the enablement requirement. Applicants respectfully traverse this rejection.

Applicants have amended Claim 42 to recite that the human cell populations are tumor cells. The use of human tumor cells is clearly enabled by the Specification, wherein experiments using tumor cells from several tumor types have beenbused, including breast epithelial, lung fibrosarcoma and human melanoma. See Examples 4 and 6.

The Examiner has rejected claims 28-40 under 35 U.S.C. §112, first paragraph, as allegedly failing to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make **and/or** use the invention (emphasis is that of the Examiner). Applicants respectfully traverse this rejection.

A determination of enabling disclosure involves an assessment of the factors enumerated in Ex Parte Forman 130 U.S.P.Q. 546 (BPAI 1986). These factors include the breadth of the claims, the state of the prior art, the amount of direction or guidance provided, and the presence or absence of working examples, all of which the Examiner has commented on in his remarks.

Regarding the breadth of the claims, The Examiner argues that the claims encompass a method dealing with ***any*** human target cell population by increasing the number of functional human IFNAR2c receptor chains on the surface of cells by ***any means***. Claim 28, as amended,

recites a method of increasing the inhibition of cell proliferation in a "human ***tumor*** target cell population ....., said method comprising ***introducing an exogenous polynucleotide encoding a human IFNAR2c polypeptide*** directly into cells of said target cell population.....". Applicants assert that the breadth of amended Claim 28 is fully enabled by the Specification.

In particular, Applicants' disclosure demonstrates the ability to introduce an exogenous polynucleotide encoding a human IFNAR2c polypeptide into several different types of human tumor cells. It provides assay methods to allow determination of the relative number of IFNAR2c polypeptides on cell surfaces (see Specification, page 13, lines 23-30) and assays to determine anti-proliferative effects of IFN treatment. It also demonstrates that human tumor cells in which the levels of surface IFNAR2c have been increased display an increased sensitivity to the antiproliferative effects of a type I IFN *in vitro* (see Specification, Example 4) and that tumors derived from such cells show reduced tumor growth *in vivo* when the animals are treated with a type I IFN (see Specification, Example 6).

Information about the state of the art that is relevant to the analysis of whether the invention is fully enabled or whether undue experimentation would have been required concerns whether those skilled in the art would be sufficiently familiar with the methods needed to practice the invention. The Examiner states that at the effective filing date of the present application, little was known about the claimed invention. Applicant's experiments have provided the information necessary to enable the invention and the amount of experimentation remaining would not be considered undue by one skilled in the art.

As noted above, Applicants' disclosure has clearly enabled one skilled in the art to introduce an exogenous polynucleotide encoding a human IFNAR2c polypeptide into human tumor cells, and shown that these cells display an increased sensitivity to the anti-proliferative effects of a type I IFN, in both *in vitro* and *in vivo* settings. These working examples are adequate to enable the complete scope of the claimed invention and would be recognized by the skilled worker as reasonably correlating with fully *in vivo* applications. See, e.g. M.P.E.P. 2164.02. For example, the Specification discloses that the claimed invention can be used both for treatment of proliferative cell conditions upon *in vivo* introduction of the IFNAR2c coding sequence into cells and also by using cells modified *in vitro*, which are subsequently transferred to the targeted tumor cell population *in vivo*, providing an anti-growth effect via a bystander effect, wherein the type I IFN acts on the modified cells to elicit the secretion of a factor which has an anti-growth effect on adjacent cells. See Specification, Page 2, lines 24-28 and Page 7, lines 23-30.

Applicants assert that with the amendment of Claim 28, the rejection by the Examiner is no longer appropriate and respectfully request its' withdrawal.

Rejection under 35 U.S.C. §112, second paragraph

Claims 28-40 and 42 are rejected under 35 U.S.C. 112, second paragraph, for being indefinite. Applicants respectfully traverse this rejection.

Applicants believe that the amendments to Claims 28 and 42 have clarified that which the Applicants believe to be their invention. Withdrawal of this rejection is respectfully requested.

Conclusion:

Applicants believe that with the amendment of Claims 28 and 42 and the arguments presented above, the Claims are in condition for allowance.

Respectfully submitted,

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Date: February 28, 2006